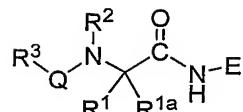


\* Attorney Docket No. 1491PCT

### What is Claimed:

### 1. A compound of Formula (I):



(I)

wherein:

5 Q is  $-\text{CO}-$ ,  $-\text{SO}_2-$ ,  $-\text{OCO}-$ ,  $-\text{NR}^4\text{CO}-$ ,  $-\text{NR}^4\text{SO}_2-$ , or  $-\text{CHR}-$  where R is haloalkyl and  $\text{R}^4$  is hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, or aralkyl;

E is:

(i)  $-\text{C}(\text{R}^5)(\text{R}^6)\text{X}^1$  where  $\text{X}^1$  is  $-\text{C}(\text{R}^7)(\text{R}^8)\text{R}^{10}$ ,  $-\text{CH}=\text{CHS}(\text{O})_2\text{R}^{10}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{R}^7)(\text{R}^8)\text{OR}^{10}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{CH}_2\text{OR}^{10}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{CH}_2\text{N}(\text{R}^{11})\text{SO}_2\text{R}^{10}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{O})\text{N}(\text{R}^{11})(\text{CH}_2)_2\text{OR}^{11}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{O})\text{NR}^{10}\text{R}^{11}$  or  $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{O})\text{N}(\text{R}^{11})(\text{CH}_2)_2\text{NR}^{10}\text{R}^{11}$ ;

(ii)  $-\text{C}(\text{R}^{5a})(\text{R}^{6a})\text{CN}$ :

where:

$R^5$  and  $R^{5a}$  are independently hydrogen or alkyl:

15         $R^6$  and  $R^{6a}$  are independently selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, -alkylene- $X^2$ - $R^{12}$  (where  $X^2$  is  $-O-$ ,  $-NR^{13}-$ ,  $-S(O)_{n1}-$ ,  $-CONR^{13}-$ ,  $-NR^{13}CO-$ ,  $-NR^{13}C(O)O-$ ,  $-NR^{13}CONR^{13}-$ ,  $-OCONR^{13}-$ ,  $-NR^{13}SO_2-$ ,  $-SO_2NR^{13}-$ ,  $-NR^{13}SO_2NR^{13}-$ ,  $-CO-$ , or  $-OC(O)-$  where  $n1$  is 0-2 and each  $R^{13}$  is hydrogen or alkyl) and  $R^{12}$  20        hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl wherein the aromatic or alicyclic ring in  $R^6$  and  $R^{6a}$  is optionally substituted with one, two, or three  $R^a$  independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monsubstituted amino, disubstituted amino, nitro, aryloxy, benzyloxy, acyl, 25        alkylsulfonyl, or arylsulfonyl where the aromatic or alicyclic ring in  $R^a$  is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl; or

$R^5$  and  $R^6$  and  $R^{5a}$  and  $R^{6a}$  taken together with the carbon atom to which both  $R^5$  and  $R^6$  and  $R^{5a}$  and  $R^{6a}$  are attached form (i) cycloalkylene optionally substituted with one or two  $R^b$  independently selected from alkyl, halo, alkylamino, dialkylamino, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, alkoxycarbonyl, or aryloxycarbonyl or (ii)

Attorney Docket No. 1491PCT

heterocycloalkylene optionally substituted with one to four alkyl or one or two R<sup>c</sup> independently selected from alkyl, haloalkyl, hydroxy, hydroxyalkyl, alkoxyalkyl, alkoxyalkyloxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, cycloalkyl, cycloalkylalkyl, -S(O)<sub>n2</sub>R<sup>14</sup>, -alkylene-S(O)<sub>n2</sub>-R<sup>15</sup>, -COOR<sup>16</sup>, -alkylene-COOR<sup>17</sup>, -CONR<sup>18</sup>R<sup>19</sup>, or -alkylene-CONR<sup>20</sup>R<sup>21</sup> (where n2 is 0-2 and R<sup>14</sup>-R<sup>17</sup>, R<sup>18</sup> and R<sup>20</sup> are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, or heterocycloalkyl and R<sup>19</sup> and R<sup>21</sup> are independently hydrogen or alkyl) wherein the aromatic or alicyclic ring in the groups attached to cycloalkylene or heterocycloalkylene is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, benzyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monosubstituted amino, disubstituted amino, or acyl;

R<sup>7</sup> is hydrogen or alkyl;

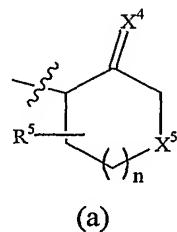
R<sup>8</sup> is hydroxy; or

R<sup>7</sup> and R<sup>8</sup> together form oxo;

R<sup>10</sup> is alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl wherein the aromatic or alicyclic ring in R<sup>10</sup> is optionally substituted with one, two, or three R<sup>d</sup> independently selected from alkyl, haloalkyl, alkoxy, alkoxyalkyl, cycloalkyl, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, aminosulfonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, aryl, aralkyl, heteroaryl, amino, monosubstituted amino, disubstituted amino, carbamoyl, or acyl and wherein the aromatic or alicyclic ring in R<sup>d</sup> is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, alkoxy, haloalkoxy, halo, hydroxy, carboxy, alkoxycarbonyl, amino, alkylamino, or dialkylamino; and

R<sup>11</sup> is hydrogen or alkyl; or

(iii) a group of formula (a):



where:

n is 0, 1, or 2;

X<sup>4</sup> is selected from -NR<sup>22</sup>-, -S-, or -O- where R<sup>22</sup> is hydrogen, alkyl, or alkoxy; and

Attorney Docket No. 1491PCT

$X^5$  is  $-O-$ ,  $-S-$ ,  $-SO_2-$ , or  $-NR^{23}-$  where  $R^{23}$  is selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl,  $-S(O)_2R^{24}$ ,  $-alkylene-S(O)_{n3}R^{25}$ ,  $-COOR^{26}$ ,

5  $-alkylene-COOR^{27}$ ,  $-CONR^{28}R^{29}$ , or  $-alkylene-CONR^{30}R^{31}$  (where  $n3$  is 0-2 and  $R^{24}-R^{27}$ ,  $R^{28}$  and  $R^{30}$  are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl and  $R^{29}$  and  $R^{31}$  are independently hydrogen or alkyl) where the aromatic or alicyclic ring in  $R^{23}$  is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, 10 alkoxy, haloalkoxy, halo, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl and one substituent selected from aryl, aralkyl, heteroaryl, or heteroaralkyl; and

$R^5$  is as defined above;

$R^1$  is hydrogen or alkyl;

15  $R^{1a}$  is 1,1-dialkylsilyl-4-ylalkylene or  $-(alkylene)-SiR^{32}R^{33}R^{34}$  where  $R^{32}$  is alkyl,  $R^{33}$  is alkyl, and  $R^{34}$  is alkyl, alkenyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, or heterocycloalkylalkyl or  $R^{33}$  and  $R^{34}$  together with Si form a heterocycloalkylene ring containing the Si atom and 3 to 7 carbon ring atoms wherein one or two carbon ring atoms are optionally independently replaced with  $-NH-$ ,  $-O-$ ,  $-S-$ ,  $-SO-$ ,  $-SO_2-$ ,  $-CO-$ ,  $-CONH-$ , or  $-SO_2NH-$  and wherein the aralkyl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylene ring in  $R^{1a}$  is optionally substituted on the ring with one, two, or three  $R^e$  independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monosubstituted amino, disubstituted amino, nitro, aryloxy, benzyloxy, acyl, alkylsulfonyl, or arylsulfonyl and further wherein the aromatic or alicyclic ring in  $R^e$  is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, 20 haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl;

25  $R^{1a}$  is 1,1-dialkylsilyl-4-ylalkylene or  $-(alkylene)-SiR^{32}R^{33}R^{34}$  where  $R^{32}$  is alkyl,  $R^{33}$  is alkyl, and  $R^{34}$  is alkyl, alkenyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, or heterocycloalkylalkyl or  $R^{33}$  and  $R^{34}$  together with Si form a heterocycloalkylene ring containing the Si atom and 3 to 7 carbon ring atoms wherein one or two carbon ring atoms are optionally independently replaced with  $-NH-$ ,  $-O-$ ,  $-S-$ ,  $-SO-$ ,  $-SO_2-$ ,  $-CO-$ ,  $-CONH-$ , or  $-SO_2NH-$  and wherein the aralkyl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylene ring in  $R^{1a}$  is optionally substituted on the ring with one, two, or three  $R^e$  independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monosubstituted amino, disubstituted amino, nitro, aryloxy, benzyloxy, acyl, alkylsulfonyl, or arylsulfonyl and further wherein the aromatic or alicyclic ring in  $R^e$  is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl;

$R^2$  is hydrogen or alkyl;

$R^3$  is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, or  $-alkylene-X^6-R^{35}$  [wherein  $X^6$  is  $-NR^{36}-$ ,  $-O-$ ,  $-S(O)_{n4}-$ ,  $-CO-$ ,  $-COO-$ ,  $-OCO-$ ,  $-NR^{36}CO-$ ,  $-CONR^{36}-$ ,  $-NR^{36}SO_2-$ ,  $-SO_2NR^{36}-$ ,  $-NR^{36}COO-$ ,  $-OCONR^{36}-$ ,  $-NR^{36}CONR^{37}-$ , or  $-NR^{36}SO_2NR^{37}-$  (where each  $R^{36}$  and  $R^{37}$  is independently hydrogen, alkyl, or acyl and  $n4$  is 0-2) and  $R^{35}$  is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl] wherein the alkylene chain in  $R^3$  is optionally substituted with one to four halo atoms and the aromatic and alicyclic rings in  $R^3$  are optionally substituted by one, two, or

Attorney Docket No. 1491PCT

three R<sup>f</sup> independently selected from alkyl, aminoalkyl, halo, hydroxy, alkoxy, haloalkyl, haloalkoxy, oxo, cyano, nitro, acyl, acyloxy, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryloxy, benzyloxy, carboxy, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, arylthio, 5 arylsulfonyl, arylsulfinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, aralkylaminosulfonyl, aminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, amino, monosubstituted or disubstituted amino, and further wherein the aromatic and alicyclic rings in R<sup>f</sup> are optionally substituted with one, two, 10 or three R<sup>g</sup> wherein R<sup>g</sup> is independently selected from alkyl, halo, haloalkyl, haloalkoxy, hydroxy, nitro, cyano, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, alkylthio, alkylsulfonyl, amino, monosubstituted amino, dialkylamino, aryl, heteroaryl, cycloalkyl, carboxy, carboxamido, or alkoxycarbonyl; or a pharmaceutically acceptable salts thereof.

15 2. The compound of Claim 1 wherein E is -CHR<sup>6</sup>C(O)R<sup>10</sup> where R<sup>6</sup> is alkyl and R<sup>10</sup> is heteroaryl optionally substituted with one or two R<sup>d</sup> independently selected from alkyl, haloalkyl, alkoxy, alkoxyalkyl, cycloalkyl, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, aryl, heteroaryl, amino, monosubstituted amino, disubstituted amino, or acyl wherein the aromatic or alicyclic ring in R<sup>d</sup> is optionally substituted with one, two, or three 20 substituents independently selected from alkyl, haloalkyl, alkoxy, haloalkoxy, halo, hydroxy, carboxy, alkoxycarbonyl, amino, alkylamino, or dialkylamino.

3. The compound of Claim 1 wherein E is -CR<sup>5a</sup>R<sup>6a</sup>CN wherein R<sup>5a</sup> and R<sup>6a</sup> together with the carbon atom to which they are attached form cycloalkylene optionally substituted with one or two R<sup>b</sup> independently selected from alkyl, halo, dialkylamino, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, alkoxycarbonyl, or aryloxycarbonyl.

25 4. The compound of Claim 1 wherein E is -CR<sup>5a</sup>R<sup>6a</sup>CN wherein R<sup>5a</sup> and R<sup>6a</sup> together with the carbon atom to which they are attached form cyclopropyl.

5. The compound of any one of the Claims 2-4 wherein R<sup>1</sup> and R<sup>2</sup> are hydrogen and Q is -CO-.

30 6. The compound of any one of the Claims 2-5 wherein R<sup>1a</sup> is -(alkylene)-SiR<sup>32</sup>R<sup>33</sup>R<sup>34</sup> where R<sup>32</sup> is alkyl, R<sup>33</sup> is alkyl, and R<sup>34</sup> is alkyl.

7. The compound of any one of the Claims 2-5 wherein R<sup>1a</sup> is -(alkylene)-SiR<sup>32</sup>R<sup>33</sup>R<sup>34</sup> where R<sup>32</sup> and R<sup>33</sup> are alkyl and R<sup>34</sup> is aralkyl.

35 8. The compound of any one of the Claims 2-7 wherein R<sup>3</sup> is heterocycloalkyl, aryl, or heteroaryl optionally substituted with one or two R<sup>f</sup>.

Attorney Docket No. 1491PCT

9. The compound of any of the Claims 2-7 wherein R<sup>3</sup> is morpholin-4-yl, 1-ethylpiperazin-4-yl, phenyl optionally substituted with one or two substituents independently selected from halo, alkoxy, alkyl, haloalkoxy, phenyl, alkylsulfonyl, haloalkyl, heteroaryl, cyano, acyl, hydroxyalkyl, or alkoxy carbonyl.

5 10. A compound selected from the group consisting of:  
morpholine-4-carboxylic acid {1(R)-[1(S)-(benzoxazol-2-ylcarbonyl)-butylcarbamoyl]-2-trimethylsilanylethyl} amide;  
morpholine-4-carboxylic acid {1(R)-[1(S)-(benzoxazol-2-ylcarbonyl)-propylcarbamoyl]-2-trimethylsilanylethyl} amide;  
10 morpholine-4-carboxylic acid {1(R)-[1(R)-(benzoxazol-2-ylcarbonyl)-propylcarbamoyl]-2-trimethylsilanylethyl} amide;  
morpholine-4-carboxylic acid {1(R)-[1(S)-(benzoxazol-2-ylcarbonyl)-pentylcarbamoyl]-2-trimethylsilanylethyl} amide;  
morpholine-4-carboxylic acid {1(R)-[1(S)-(5-chlorobenzoxazol-2-ylcarbonyl)-propylcarbamoyl]-2-trimethylsilanylethyl} amide;  
15 morpholine-4-carboxylic acid {1(S)-[1(S)-(benzoxazol-2-ylcarbonyl)-propylcarbamoyl]-2-trimethylsilanylethyl} amide;  
morpholine-4-carboxylic acid {1(R)-[1(S)-(benzoxazol-2-ylcarbonyl)-butylcarbamoyl]-2-trimethylsilanylethyl} amide;  
morpholine-4-carboxylic acid {1(R)-[1(S)-(benzoxazol-2-ylcarbonyl)-butylcarbamoyl]-2-trimethylsilanylethyl} amide;  
20 1-(R)-morpholine-4-carboxylic acid [1-(1-cyanocyclopropylcarbamoyl)-2-(trimethylsilyl)-ethyl] amide  
1-(R)-morpholine-4-carboxylic acid [1-(4-cyano-1-ethylpiperidin-4-ylcarbamoyl)-2-(trimethylsilyl)ethyl] amide;  
1-(R)-morpholine-4-carboxylic acid [1-(4-cyano-1,1-dioxohexahydro-1<sup>λ</sup><sup>6</sup>-thiopyran-4-yl-carbamoyl)-2-(trimethylsilyl)ethyl] amide;  
25 morpholine-4-carboxylic acid [1-(RS)-(1-benzyloxymethyl-1-cyanopropylcarbamoyl)-2-trimethyl-silanylethyl] amide;  
morpholine-4-carboxylic acid [1-(RS)-(2-benzyloxy-1-cyano-1-methyl-ethylcarbamoyl)-2-trimethylsilanylethyl] amide;  
30 4-ethylpiperazine-1-carboxylic acid [1-(RS)-(1-cyanocyclopropylcarbamoyl)-2-trimethyl-silanylethyl] amide;  
3'-methoxybiphenyl-3-carboxylic acid [1-(R)-(1-cyano-cyclopropylcarbamoyl)-2-trimethylsilanylethyl] amide;  
*N*-[1-(RS)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]-3-iodobenzamide;

Attorney Docket No. 1491PCT

3'-trifluoromethoxybiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

biphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

5 2',6'-dimethoxybiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

4'-methylsulfonylbiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

2'-chlorobiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

10 3'-methylbiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

2'-trifluoromethylbiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

3'-methylbiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

15 3'-trifluoromethoxybiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

*N*-[1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]-3-pyridin-3-ylbenzamide;

3'-cyanobiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

20 3'-hydroxymethylbiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

4'-hydroxymethylbiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

2'-methylbiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

25 3'-methoxycarbonylbiphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

4'-acetyl biphenyl-3-carboxylic acid [1-(*RS*)-(1-cyanocyclopropylcarbamoyl)-2-trimethylsilanylethyl]amide;

30 3'-methoxybiphenyl-3-carboxylic acid [1-(*RS*)-(4-cyano-4-tetrahydrothiopyran-4-ylcarbamoyl)-2-trimethylsilanylethyl]amide;

3'-methoxybiphenyl-3-carboxylic acid [1-(*RS*)-(4-cyano-1,1-dioxohexahydro-1*λ*<sup>6</sup>-thiopyran-4-yl-carbamoyl)-2-(trimethylsilanyl)ethyl]amide; and

35 1-[3-(benzyldimethylsilanyl)-2*R*-(2,2,2-trifluoro-1-phenylethylamino)propionyl]cyclopropane-carbonitrile; or

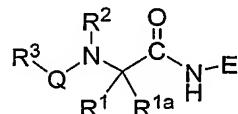
Attorney Docket No. 1491PCT

a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition comprising a compound of any of the Claims 1-10 and a pharmaceutically acceptable excipient.

12. A method for treating a disease in an animal mediated by cysteine proteases which

5 method comprises administering to the animal a therapeutically effective amount of a compound of Formula (I):



(I)

where:

10 Q is  $-\text{CO}-$ ,  $-\text{SO}_2-$ ,  $-\text{OCO}-$ ,  $-\text{NR}^4\text{CO}-$ ,  $-\text{NR}^4\text{SO}_2-$ , or  $-\text{CHR}-$  where R is haloalkyl and  $\text{R}^4$  is hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, or aralkyl;

E is:

(i)  $-\text{C}(\text{R}^5)(\text{R}^6)\text{X}^1$  where  $\text{X}^1$  is  $-\text{CHO}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{CF}_3$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{CF}_2\text{CF}_2\text{R}^9$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{R}^{10}$ ,  $-\text{CH}=\text{CHS}(\text{O})_2\text{R}^{10}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{R}^7)(\text{R}^8)\text{OR}^{10}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{CH}_2\text{OR}^{10}$ ,  
15  $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{R}^7)(\text{R}^8)\text{R}^{10}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{CH}_2\text{N}(\text{R}^{11})\text{SO}_2\text{R}^{10}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{CF}_2\text{C}(\text{O})\text{NR}^{10}\text{R}^{11}$ ,  
 $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{O})\text{NR}^{10}\text{R}^{11}$ ,  $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{O})\text{N}(\text{R}^{11})(\text{CH}_2)_2\text{OR}^{11}$ , or  
 $-\text{C}(\text{R}^7)(\text{R}^8)\text{C}(\text{O})\text{N}(\text{R}^{11})(\text{CH}_2)_2\text{NR}^{10}\text{R}^{11}$ ;

(ii)  $-\text{C}(\text{R}^{5a})(\text{R}^{6a})\text{CN}$ ;

where:

20  $\text{R}^5$  and  $\text{R}^{5a}$  are independently hydrogen or alkyl;

$\text{R}^6$  and  $\text{R}^{6a}$  are independently selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, -alkylene- $\text{X}^2\text{-R}^{12}$  (where  $\text{X}^2$  is  $-\text{O}-$ ,  $-\text{NR}^{13}-$ ,  $-\text{S}(\text{O})_{n1}-$ ,  $-\text{CONR}^{13}-$ ,  $-\text{NR}^{13}\text{CO}-$ ,  $-\text{NR}^{13}\text{C}(\text{O})\text{O}-$ ,  $-\text{NR}^{13}\text{CONR}^{13}-$ ,  $-\text{OCONR}^{13}-$ ,  $-\text{NR}^{13}\text{SO}_2-$ ,  $-\text{SO}_2\text{NR}^{13}-$ ,  $-\text{NR}^{13}\text{SO}_2\text{NR}^{13}-$ ,  $-\text{CO}-$ , or  $-\text{OC}(\text{O})-$  where  $n1$  is 0-2 and each  $\text{R}^{13}$  is hydrogen or alkyl) and  $\text{R}^{12}$

25 hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl wherein the aromatic or alicyclic ring in  $\text{R}^6$  and  $\text{R}^{6a}$  is optionally substituted with one, two, or three  $\text{R}^a$  independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxy carbonyl,

30 amino, monosubstituted amino, disubstituted amino, nitro, aryloxy, benzyloxy, acyl, alkylsulfonyl, or arylsulfonyl where the aromatic or alicyclic ring in  $\text{R}^a$  is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy,

Attorney Docket No. 1491PCT

haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl; or

$R^5$  and  $R^6$  and  $R^{5a}$  and  $R^{6a}$  taken together with the carbon atom to which both  $R^5$  and  $R^6$  and  $R^{5a}$  and  $R^{6a}$  are attached form (i) cycloalkylene optionally substituted with one or two  $R^b$

5 independently selected from alkyl, halo, alkylamino, dialkylamino, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, alkoxycarbonyl, or aryloxycarbonyl or (ii) heterocycloalkylene optionally substituted with one to four alkyl or one or two  $R^c$  independently selected from alkyl, haloalkyl, hydroxy, hydroxyalkyl, alkoxyalkyl, alkoxyalkyloxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, cycloalkyl, cycloalkylalkyl,  $-S(O)_{n2}R^{14}$ ,  $-alkylene-S(O)_{n2}R^{15}$ ,  $-COOR^{16}$ ,  $-alkylene-COOR^{17}$ ,  $-CONR^{18}R^{19}$ , or  $-alkylene-CONR^{20}R^{21}$  (where  $n2$  is 0-2 and  $R^{14}$ - $R^{17}$ ,  $R^{18}$  and  $R^{20}$  are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, or heterocycloalkyl and  $R^{19}$  and  $R^{21}$  are independently hydrogen or alkyl) wherein the aromatic or alicyclic ring in the groups attached to cycloalkylene or heterocycloalkylene is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, benzyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monosubstituted amino, disubstituted amino, or acyl;

10  $R^7$  is hydrogen or alkyl;

20  $R^8$  is hydroxy; or

$R^7$  and  $R^8$  together form oxo;

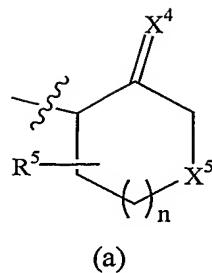
$R^9$  is hydrogen, halo, alkyl, aralkyl or heteroaralkyl;

25  $R^{10}$  is alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl wherein the aromatic or alicyclic ring in  $R^{10}$  is optionally substituted with one, two, or three  $R^d$  independently selected from alkyl, haloalkyl, alkoxy, alkoxyalkyl, cycloalkyl, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, aminosulfonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, aryl, aralkyl, heteroaryl, amino, monosubstituted amino, disubstituted amino, carbamoyl, or acyl and wherein the aromatic or alicyclic ring in  $R^d$  is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, alkoxy, haloalkoxy, halo, hydroxy, carboxy, alkoxycarbonyl, amino, alkylamino, or dialkylamino; and

30  $R^{11}$  is hydrogen or alkyl; or

(iii) a group of formula (a):

Attorney Docket No. 1491PCT



where:

n is 0, 1, or 2;

5  $X^4$  is selected from  $-NR^{22}-$ ,  $-S-$ , or  $-O-$  where  $R^{22}$  is hydrogen, alkyl, or alkoxy; and  
 $X^5$  is  $-O-$ ,  $-S-$ ,  $-SO_2-$ , or  $-NR^{23}-$  where  $R^{23}$  is selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl,  $-S(O)_2R^{24}$ ,  $-alkylene-S(O)_{n3}-R^{25}$ ,  $-COOR^{26}$ ,  $-alkylene-COOR^{27}$ ,  $-CONR^{28}R^{29}$ , or  $-alkylene-CONR^{30}R^{31}$  (where  $n3$  is 0-2 and  $R^{24}$ -  
10  $R^{27}$ ,  $R^{28}$  and  $R^{30}$  are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl and  $R^{29}$  and  $R^{31}$  are independently hydrogen or alkyl) where the aromatic or alicyclic ring in  $R^{23}$  is  
optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, alkoxy, haloalkoxy, halo, hydroxy, amino, alkylamino, dialkylamino, carboxy, or  
15 alkoxycarbonyl and one substituent selected from aryl, aralkyl, heteroaryl, or heteroaralkyl; and

 $R^5$  is as defined above; $R^1$  is hydrogen or alkyl;

20  $R^{1a}$  is 1,1-dialkylsilinan-4-ylalkylene or  $-(alkylene)-SiR^{32}R^{33}R^{34}$  where  $R^{32}$  is alkyl,  $R^{33}$  is alkyl, and  $R^{34}$  is alkyl, alkenyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, or heterocycloalkylalkyl or  $R^{33}$  and  $R^{34}$  together with Si form a heterocycloalkylene ring containing the Si atom and 3 to 7 carbon ring atoms wherein one or two carbon ring atoms are optionally independently replaced with  $-NH-$ ,  $-O-$ ,  $-S-$ ,  $-SO-$ ,  $-SO_2-$ ,  $-CO-$ ,  $-CONH-$ , or  $-SO_2NH-$  and wherein the aralkyl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylene ring in  $R^{1a}$  is optionally substituted on the ring with one, two, or three  $R^e$  independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monosubstituted amino, disubstituted amino, nitro, aryloxy, benzyloxy, acyl, alkylsulfonyl, or arylsulfonyl and further wherein the aromatic or alicyclic ring in  $R^e$  is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl;  
25  $R^2$  is hydrogen or alkyl;

\* Attorney Docket No. 1491PCT

R<sup>3</sup> is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, or -alkylene-X<sup>6</sup>-R<sup>35</sup> [wherein X<sup>6</sup> is -NR<sup>36</sup>-, -O-, -S(O)<sub>n4</sub>-, -CO-, -COO-, -OCO-, -NR<sup>36</sup>CO-, -CONR<sup>36</sup>-, -NR<sup>36</sup>SO<sub>2</sub>-, -SO<sub>2</sub>NR<sup>36</sup>-, -NR<sup>36</sup>COO-, -OCONR<sup>36</sup>-, -NR<sup>36</sup>CONR<sup>37</sup>-, or -NR<sup>36</sup>SO<sub>2</sub>NR<sup>37</sup>- (where each R<sup>36</sup> and R<sup>37</sup> is independently hydrogen, alkyl, or acyl and n4 is 0-2) and R<sup>35</sup> is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl] wherein the alkylene chain in R<sup>3</sup> is optionally substituted with one to four halo atoms and the aromatic and alicyclic rings in R<sup>3</sup> are optionally substituted by one, two, or three R<sup>f</sup> independently selected from alkyl, aminoalkyl, halo, hydroxy, alkoxy, haloalkyl, 10 haloalkoxy, oxo, cyano, nitro, acyl, acyloxy, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryloxy, benzyloxy, carboxy, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, arylthio, arylsulfonyl, arylsulfinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, 15 dialkylaminosulfonyl, arylaminosulfonyl, aralkylaminosulfonyl, aminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, amino, monosubstituted or disubstituted amino, and further wherein the aromatic and alicyclic rings in R<sup>f</sup> are optionally substituted with one, two, or three R<sup>g</sup> wherein R<sup>g</sup> is independently selected from alkyl, halo, haloalkyl, haloalkoxy, hydroxy, nitro, cyano, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, alkylthio, alkylsulfonyl, 20 amino, monosubstituted amino, dialkylamino, aryl, heteroaryl, cycloalkyl, carboxy, carboxamido, or alkoxycarbonyl; or a pharmaceutically acceptable salts thereof.

14. The method of Claim 13 wherein the cysteine protease is Cathepsin S.

15. The method of Claim 14 wherein the disease is an psoriasis, autoimmune disorder,

25 allergic disorder, chronic obstructive pulmonary disease, or cardiovascular disease.

16. Use of a compound of Claim 1 in the preparation of a medicament.

17. Use of a compound of Claim 1 in the preparation of a medicament for the treatment of a disease mediated by Cathepsin S.